REMARKS

The claims

Claims 41-58 are currently pending in the application. Claims 43-46 and 48 have been cancelled without prejudice or disclaimer. Applicants reserve the right to pursue claims of corresponding subject matter in subsequently filed applications. Claims 41, 42, 47 and 49-53 have been amended in order to place them in better condition for allowance or appeal. Support for the amendments is found for example at p. 17, lines 1-9 of the specification. It is maintained that the claim amendments do not introduce new matter or raise new issues requiring further consideration and/or search. Entry of the amendments is respectfully requested. Claim 41, 42, 47 and 49-58 are currently pending in the application.

Rejections under 35 U.S.C. 112

Claims 41-46, 48, 49 and 53-58 are rejected under 35 U.S.C. 112, first paragraph. The Examiner argues that the specification is enabled for an unfused human OPG polypeptide of residues 22-401 and for unfused murine OPG polypeptides of residues 22-194, 22-200, 22-201, 22-293 and 22-355 based on the allegation that only these OPG constructs have been previously shown to have activity (citing Table 1 of PCT publication no. WO97/23614). Applicants disagree.

Applicants maintain that the Examiner continues to misrepresent the contents of Table 1 of PCT publication no. WO97/23614 as explained in the response dated August 7, 2003. For example, Table 1 clearly shows that truncated human OPG of residues 22 to 194 and 22 to 201 is biologically active. As previously stated, there are numerous other examples of OPG constructs which are biologically active which were not cited by the Examiner. It is incorrect for the Examiner to assert that the present application only enables unfused truncated murine OPG polypeptides.

Moreover, Applicant notes that co-pending U.S. application no. 09/389,782 (the "'782 application") filed September 3, 1999 the contents of which are incorporated by reference into the present application, gives several examples of unfused and fused human OPG polypeptides which are biologically active. See, for example, Tables 2, 3 and 4 in Example 2 of the '782 application. The '782 application was filed on the same day as the present application and the examples contained therein also enable the scope of the claims.

Claim 43 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for recitation of the "mature" form of OPG. Applicant has cancelled Claim 43 without prejudice or disclaimer thereby rendering the rejection moot.

Claims 42-47 and 56-58 are rejected under 35 U.S.C. 112, first paragraph, as the specification allegedly does not describe a method for preventing abnormal bone formation associated with cancer.

In the response of August 7, 2003, Applicants have pointed to ample support in the specification for Claim 42 and claims depending therefrom. The Examiner argues that the disclosure at p. 30, lines 32-36, for example, should be limited to OPG fusion polypeptides. Applicants maintain that this is a narrow reading of one sentence of the specification that improperly limits what is disclosed throughout the application. It is clear that both OPG polypeptides and OPG fusion polypeptides may be employed in the claimed methods as stated at p. 5, lines 26-32:

> OPG polypeptides of the invention encompass those polypeptides which have the activity of inhibiting bone resorption and may be used to prevent and/or treat loss of bone mass or prevent osteosclerotic bone metastasis (replacement of structurally sound bone with disorganized structurally deficient bone). In preferred embodiments, OPG polypeptides are fusion proteins comprising OPG and a heterologus [sic] peptide or protein.

The term "OPG polypeptide" refers to both fused and unfused OPG polypeptides (see p. 8, lines 17-27). It is clear that the Applicants contemplated the use of both fused and unfused OPG polypeptides to prevent osteosclerotic bone metastasis.

Without acquiescing to the rejection and solely to advance prosecution, Applicant has amended the claims to recite OPG fusion polypeptides.

Rejection under 35 U.S.C. 103

Claims 41-58 are rejected under 35 U.S.C. 103 as being obvious over Boyle et al. (PCT publication no. WO97/23614) in view of Conte et al. (Annals of Oncology 5, S41-S44 (1994)) and Simonet et al. (Cell 89, 309-319 (1997)). The Examiner argues that the combination of OPG with a cancer therapy agent for the treatment of bone loss associated with cancer would have been obvious because "the art recognized OPG for treatment of bone loss associated with cancer and chemotherapy in combination with bone loss prevention molecules." The Examiner also argues that the rejection is not based on hindsight if it does not rely on knowledge set forth in Applicant's own disclosure.

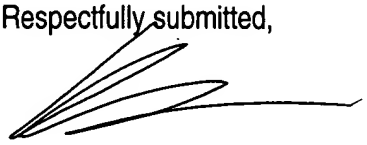
Applicants maintain that while it may have been obvious to use OPG with a cancer therapy agent for the treatment of bone loss, it would have been unexpected that the claimed OPG fusion polypeptides of

at least about amino acid residues 22 to 194 as shown in Figure 2 (SEQ ID NO:2) could be used in combination with a cancer therapy agent. It is requested that the rejection be withdrawn.

CONCLUSION

Claims 41, 42, 47 and 49-58 are in condition for allowance and an early notice thereof is solicited.

Respectfully submitted,



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